STIC-Biotech/ChemLib 137819 MEI

From: Chan, Christina
Sent: Monday, November 15, 2004 1:08 PM
To: Basi, Nirmal; STIC-Biotech/ChemLib
Subject: RE: Rush search for App. #: 10/016,496

Please rush Thanks Chris

Chris Chan
TC 1600 New Hire Training Coordinator and SPE 1644
(571)-272-0841
Remsen, 3E89

-----Original Message-----
From: Basi, Nirmal
Sent: Monday, November 15, 2004 12:58 PM
To: Chan, Christina
Subject: Rush search for App. #: 10/016,496

Christina I am seeking approval for a RUSH sequence search, as indicated below. The case is on my amended docket. If approved, could you please forward the search to STIC and cc a copy to me.

Examiner: Nirmal S. Basi
Art Unit 1646
Office: Remsen Building, Room 4D68
Mail Room: Remsen Building, room 4C70

Sequence search:

App. #: 10/016,496
Result format: Paper.

Title:**POLYCATION-SENSING RECEPTOR IN AQUATIC SPECIES AND METHODS OF USE THEREOF**

Inventors: Harris et al

Priority Date: 3/27/96
Please search:
i) SEQ ID NO:1 and 2

Search issued, commercial and interference databases.

****
STAFF USE ONLY

Searcher: D. Schreiber
Searcher Phone: 2- 2526
Date Searcher Picked up:
Date Completed: 11/18
Searcher Prep/Rev. Time: 16
Online Time: 8

****
Type of Search
NA Sequence: # 1
AA Sequence :# 1
Structure: #
Bibliographic:
Litigation:
Patent Family:
Other:

****
Vendors and cost where applicable
STN:
DIALOG:
QUESTEL/ORBIT:
LEXIS/NEXIS:
SEQUENCE SYSTEM: Compugen
WWW/Internet:
Other(Specify):

Thanks,
Nirmal S. Basi

****
STAFF USE ONLY

Searcher:_____
Searcher Phone: 2-
Date Searcher Picked up:____
Date Completed:_____
Searcher Prep/Rev. Time:___
Online Time:_____

****
Type of Search
NA Sequence: #_____
AA Sequence :#_____
Structure: #_____
Bibliographic:_____
Litigation:_____
Patent Family:_____
Other:_____

****
Vendors and cost where applicable
STN:_____
DIALOG:_____
QUESTEL/ORBIT:_____
LEXIS/NEXIS:_____
SEQUENCE SYSTEM:_____
WWW/Internet:_____
Other(Specify):_____

```
FILE 'MEDLINE'
FILE 'JAPIO'

FILE 'BIOSIS'

FILE 'SCISEARCH'

FILE 'WPIDS'

FILE 'CAPLUS'

FILE 'EMBASE'
=> s polyvalent cation sensing receptor#
L1          108 POLYVALENT CATION SENSING RECEPTOR#

=> s aquatic pvcr#
L2            6 AQUATIC PVCR#

=> s l1 or l2
L3          108 L1 OR L2

=> s shark kidney calcium receptor related protein or skca-rp-i or skcar-i
   6 FILES SEARCHED...
L4            3 SHARK KIDNEY CALCIUM RECEPTOR RELATED PROTEIN OR SKCA-RP-I OR
                SKCAR-I

=> s l3 and l4
L5            3 L3 AND L4

=> s 209602 and atcc
L6            2 209602 AND ATCC

=> s l6 abnd l4
MISSING OPERATOR L6 ABND
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l6 and l4
L7            1 L6 AND L4

=> s l6 and l3
L8            2 L6 AND L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L9            3 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l9 ibib abs 1-3

L9   ANSWER 1 OF 3  WPIDS  COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER:      2003-845319 [78]   WPIDS
CROSS REFERENCE:       2002-426283 [45]
DOC. NO. CPI:          C2003-237582
TITLE:                 New Atlantic salmon polyvalent cation-sensing receptor,
                       PVCR, polypeptides useful in commercial raising of salmon
                       and restoration of wild Atlantic salmon populations
                       especially in transfer from freshwater to seawater.
DERWENT CLASS:         B04 C06 D16
INVENTOR(S):           BETKA, M; HARRIS, H W; NEARING, J
PATENT ASSIGNEE(S):    (MARI-N) MARICAL INC
COUNTRY COUNT:         103
PATENT INFORMATION:

     PATENT NO        KIND DATE     WEEK       LA   PG
     ------------------------------------------------
     WO 2003087331    A2 20031023 (200378)* EN  135
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
            LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL
            PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU
            ZA ZM ZW
     AU 2003232002    A1 20031027 (200436)
```

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003087331	A2	WO 2003-US11188	20030409
AU 2003232002	A1	AU 2003-232002	20030409

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003232002	A1 Based on	WO 2003087331

PRIORITY APPLN. INFO: US 2002-125792 20020418; US 2002-121441 20020411; US 2002-125772 20020418; US 2002-125778 20020418

AN 2003-845319 [78] WPIDS

CR 2002-426283 [45]

AB WO2003087331 A UPAB: 20040608

NOVELTY - An isolated polypeptide having at least 80 % identity to one of sequences (I)-(IV) for Atlantic salmon PVCRs SalmoKCaR1, 2, 3 or 4 respectively (or functional fragment of (I), (II), (III) or (IV) or encoded by one of sequences (V)-(VIII) encoding (I)-(IV) respectively), is new.

DETAILED DESCRIPTION - An isolated polypeptide having at least 80 % identity to one of sequences (I)-(IV) for Atlantic salmon PVCRs SalmoKCaR1, 2, 3 or 4 respectively (or functional fragment of (I), (II), (III) or (IV) or encoded by one of sequences (V)-(VIII) encoding (I)-(IV) respectively), is new.

The polypeptide allows for/assists in one or more functions in Atlantic salmon as follows:

(a) sensing/adapting to SalmoKCaR modulator(s) in serum or the surrounding environment;

(b) imprinting with an odorant;

(c) altering water intake/absorption; and

(d) altering urine output.

INDEPENDENT CLAIMS are also included for:

(1) an isolated polynucleotide comprising:

(a) sequence (V), (VI), (VII) or (VIII) or its coding region;

(b) having at least 70 % identity to sequence as in (a) (or encoding functional fragment of one of (V)-(VIII)) and encoding polypeptide as above;

(c) complementary to polynucleotide having sequence (V), (VI), (VII) or (VIII), or its coding region;

(d) encoding polypeptide having sequence (I), (II), (III) or (IV) (and especially RNA);

(e) hybridizing under high stringency conditions to coding region of sequence (V), (VI) (VII) or (VIII) but not to sequence (IX) for a ***shark*** ***kidney*** ***calcium*** ***receptor*** ***related*** ***protein*** (SKCaR) or one of 10 known sequences for a fugu pheromone receptor; (vi) probes hybridizing under stringent conditions to sequence (V), (VI), (VII) or (VIII) or its coding region, but not to sequence (IX) or one of fugu pheromone receptor sequences above;

(2) vectors or plasmids comprising polynucleotide as in (1)(a), (1)(d) or (1)(e);

(3) host cells comprising polynucleotide as in (1)(a), (1)(d) or (1)(e);

(4) antibodies specifically binding polypeptide;

(5) fusion proteins comprising polypeptide (or functional fragment) and a portion of an immunoglobulin;

(6) transgenic fish comprising polynucleotide as in (1)(a)-(d); and

(7) nucleic acid (optionally DNA) probes having sequence from (V)-(VIII) but not (IX) or one of fugu pheromone receptor sequences above.

USE - The polypeptides are used to identify polypeptide modulators by contacting test compound with cell transcribing polypeptide and determining increase/decrease in polypeptide expression level/activity (and optionally increase/decrease in e.g. phosphorylation) compared to Controls. The polynucleotides are used to test for polynucleotide modulators by contacting cells expressing polynucleotide with test compound and measuring changes in one or more intracellular transduction systems altered by activation of expressed proteins or changes in expression level of polynucleotide.

The polypeptides and polynucleotides are useful in commercial raising of Atlantic salmon and restoration of wild Atlantic salmon populations, especially to enable transfer from freshwater to seawater with increased

growth and reduced mortality. For example, they can be used in testing of salmon to determine if they are ready for transfer to seawater, to enable transfer at the best time. Polypeptides can be used to alter water intake/absorption, alter urine output or imprint salmon with an odorant e.g. an attractant added to feed so that salmon later recognize and/or distinguish the odorant and consume more feed.

The polypeptide allows for/assists in functions relevant to sensing and adapting to ion concentrations in Atlantic salmon. They may be use to produce antibodies, useful to assay for SalmoKCaR receptors in samples. The polypeptides and polynucleotides can be used to identify polypeptide/polynucleotide modulators, useful e.g. to add to freshwater or feed to increase serum modulator levels to increase/decrease SalmoKCaR expression/sensitivity in preparing salmon for transfer to seawater. The polynucleotides can also be used to produce probes to assay for polynucleotides encoding SalmoKCaR in samples (claimed).

Dwg.0/49

L9 ANSWER 2 OF 3 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-163246 [21] WPIDS
CROSS REFERENCE: 1997-489640 [45]; 2003-874926 [81]
DOC. NO. CPI: C2002-050370
TITLE: New nucleic acid molecule encoding polyvalent cation-sensing receptor protein, useful for regulating adaptation of fish e.g. flounder to marine and fresh water environments, and to alter tissue or meat/muscle composition.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): BROWN, E M; HARRIS, H W; HEBERT, S C
PATENT ASSIGNEE(S): (BGHM) BRIGHAM & WOMENS HOSPITAL
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6337391	B1	20020108	(200221)*		83

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6337391	B1	CIP of	US 1996-622738	19960327
		CIP of	WO 1997-US5031	19970327
			US 1998-162021	19980928

PRIORITY APPLN. INFO: US 1998-162021 19980928; US 1996-622738 19960327; WO 1997-US5031 19970327

AN 2002-163246 [21] WPIDS
CR 1997-489640 [45]; 2003-874926 [81]
AB US 6337391 B UPAB: 20031216

NOVELTY - An isolated nucleic acid sequence (I) comprising a fully defined sequence (S1) of 4134 base pairs as given in the specification encoding polyvalent cation-sensing receptor protein (PVCR), especially ***Shark*** ***Kidney*** ***calcium*** ***receptor*** ***related*** ***protein*** -I (SKCaR-RP-I) that allows fish to sense ion concentrations with a fully defined sequence of 1027 amino acids as given in the specification or its complement, is new.

DETAILED DESCRIPTION - An isolated nucleic acid sequence (I) comprising:

(a) a fully defined sequence (S1) of 4134 base pairs as given in the specification;

(b) coding region of S1 encoding polyvalent cation-sensing receptor protein (PVCR), especially ***Shark*** ***Kidney*** ***calcium*** ***receptor*** ***related*** ***protein*** -I (SKCaR-RP-I) that allows fish to sense ion concentrations with a fully defined sequence of 1027 amino acids as given in the specification; or

(c) complement of (I), is new.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid sequence having at least 80% or 90% identity with (S1), or the coding region of (S1), and that encodes a polypeptide that allows fish to sense ion concentrations, or that assists fish in adapting to changing ion concentrations by altering water intake, water absorption or urine output, and allows fish to modulate the percentage of total fat, protein and moisture of muscle;

(2) an isolated nucleotide sequence, i.e. RNA sequence that encodes PVCR;

(3) a probe that hybridizes under high stringency conditions to (S1) or its complement, where the stringent conditions comprise 0.5 X standard saline citrate (SSC), 0.1% sodium dodecyl sulfate (SDS) and at 65 deg. C, where the probe hybridizes to a nucleic acid that encodes a polypeptide that allows fish to sense ion concentrations;
(4) a vector comprising (I) or its hybridizable sequence;
(5) a host cell transformed with the above vector; and
(6) an cDNA purified from a clone deposited under ATCC No. 209602.
USE - (I) or its fragment is useful as a probe to isolate additional aquatic PVCR homologs. (I) is useful for producing receptor proteins which can be used for structure determination, to assay a molecule's activity on a receptor, and to obtain antibodies binding to the receptor; being sequenced to determine a receptor's nucleotide sequence which can be used, as a basis for comparison with other receptors to determine conserved regions, determine unique nucleotide sequences for normal and altered receptors, and to determine nucleotide sequences to be used as target sites for antisense nucleic acids, ribozymes, hybridization detection probes, or polymerase chain reaction (PCR) amplification primers; as hybridization detection probes to detect the presence of a native receptor and/or a related receptor in a sample; and as PCR primers to generate particular nucleic acid sequence regions, for e.g. to generate regions to be probed by hybridization detection probes. The aquatic PVCR allows the successful adaptation of fish, such as flounder, to marine and fresh water environments, and controls maturation and developmental stages in marine species. Modulating the expression of PVCR activates or inhibits PVCR mediated ion transport and endocrine changes that permit fish to adapt to fresh or salt water. Activating PVCR in epithelial cells increases or decreases salinity tolerance in aquatic species. Regulating salinity tolerance is useful to develop new species of marine fish that are easily adaptable to fresh water aqua culture. The methods are useful for altering body composition i.e. tissue composition or meat/muscle composition by modulating salinity of surrounding environment. Body composition altered include fat content, protein content, weight, thickness, moisture and taste. Maintaining aquatic species in higher salinity than normal reduces parasites and/or bacteria while maintaining the species in lower salinity reduces contaminants, e.g. antibiotics, hydrocarbons and/or amines. The species can be maintained in both environments, consecutively to reduce parasites, bacteria and contaminants.
Dwg.0/32

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:650450 CAPLUS
DOCUMENT NUMBER: 127:317024
TITLE: Polycation-sensing receptors in aquatic species including cDNA sequence and screening for receptor regulators useful for marine species aquaculture and salinity tolerance regulation
INVENTOR(S): Harris, H. William; Brown, Edward; Hebert, Steven
PATENT ASSIGNEE(S): Brigham and Women's Hospital, USA; Harris, H. William; Brown, Edward; Hebert, Steven
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735977	A1	19971002	WO 1997-US5031	19970327
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2250069	AA	19971002	CA 1997-2250069	19970327
AU 9725926	A1	19971017	AU 1997-25926	19970327
EP 934407	A1	19990811	EP 1997-917662	19970327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000507822	T2	20000627	JP 1997-534639	19970327
US 6337391	B1	20020108	US 1998-162021	19980928
AU 755847	B2	20021219	AU 2000-66689	20001023
US 2003166908	A1	20030904	US 2001-16496	20011210

PRIORITY APPLN. INFO.: US 1996-622738 A2 19960327
AU 1997-25926 A3 19970327
WO 1997-US5031 W 19970327
US 1998-162021 A3 19980928
US 2000-715538 A3 20001117

AB Aquatic polyvalent cation-sensing receptor (PVCR) in elasmobranch and teleost fish and methods of regulating polycation-sensing receptor-mediated functions are described. Methods for regulating salinity tolerance and identifying substances capable of regulating ionic compns. of fish, and the role of Aquatic PVCR proteins in maintaining osmoregulation are characterized. Methods to regulate salinity tolerance in fish can facilitate aquaculture of marine fish, permitting these species to be raised initially in fresh water hatcheries and later transferred to marine conditions. The general invention is exemplified by immunohistochem. identification of PVCR in epithelial cells of various elasmobranch fish, including dogfish shark (Squalus acanthias) and little skate (Raja erinacea), in various teleost fish including winter flounder (Pseudopleuronectes americanus), fresh water trout (Onchorhynchus nerka). The ***shark*** ***kidney*** ***calcium*** ***receptor*** ***related*** ***protein*** SKCaR-RP cDNA sequence is included. Also, PVCR expression in kidney tubules of killifish (Fundulus heteroclitus) either chronically (18 days) or acutely (7 days) adapted to salt or fresh water is compared and an assay for PVCR agonists and antagonists using flounder urinary bladder is included.

=
FILE 'MEDLINE, JAPIO, BIOSIS, SCISEARCH, WPIDS, CAPLUS, EMBASE' ENTERED

L1 108 S POLYVALENT CATION SENSING RECEPTOR#
L2 6 S AQUATIC PVCR#
L3 108 S L1 OR L2
L4 3 S SHARK KIDNEY CALCIUM RECEPTOR RELATED PROTEIN OR SKCA-RP-I OR
L5 3 S L3 AND L4
L6 2 S 209602 AND ATCC
L7 1 S L6 AND L4
L8 2 S L6 AND L3
L9 3 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l6 ibib abs 1-2

L6 ANSWER 1 OF 2 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-874926 [81] WPIDS
CROSS REFERENCE: 1997-489640 [45]; 2002-163246 [21]
DOC. NO. CPI: C2003-246939
TITLE: Fish polyvalent cation-sensing receptor proteins, useful for assisting fish in adapting to changing ion concentrations by altering water intake and absorption, urine output or for modulating the fat, protein and moisture content of muscle.
DERWENT CLASS: B04 D16
INVENTOR(S): BROWN, E M; HARRIS, H W; HEBERT, S C
PATENT ASSIGNEE(S): (BGHM) BRIGHAM & WOMENS HOSPITAL
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003166908	A1	20030904	(200381)*		1

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003166908	A1 CIP of	US 1996-622738	19960327
	CIP of	WO 1997-US5031	19970327
	Div ex	US 1998-162021	19980928
	Div ex	US 2000-715538	20001117
		US 2001-16496	20011210

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2003166908	A1 Div ex	US 6337391

PRIORITY APPLN. INFO: US 1998-162021 19980928; US

1996-622738 19960327; WO
1997-US5031 19970327; US
2000-715538 20001117; US
2001-16496 20011210

AN 2003-874926 [81] WPIDS
CR 1997-489640 [45]; 2002-163246 [21]
AB US2003166908 A UPAB: 20031216

NOVELTY - Aquatic polyvalent cation-sensing receptor (PVCR) polypeptide (I), is new.

DETAILED DESCRIPTION - An isolated polypeptide (I) molecule having at least about 80 - 90% identity with:

(a) 6 defined amino acid sequences (A1-A6) given in the specification; or

(b) an amino acid sequence encoded by the defined nucleic acid sequences (N1-N6) given in the specification (the isolated polypeptide molecule:

(i) allows fish to sense ion concentrations;

(ii) assists fish in adapting to changing ion concentrations by altering water intake, water absorption or urine output; and/or

(iii) allows a fish to modulate the percentage of total fat, protein and moisture of muscle).

INDEPENDENT CLAIMS are also included for:

(1) an antibody (II) that specifically binds to (I); and

(2) screening (III) for Aquatic polyvalent cation-sensing receptor agonists and antagonists comprising measuring water reabsorption in isolated urinary bladder by:

(a) isolating flounder urinary bladder containing an Aquatic polyvalent cation-sensing receptor;

(b) weighing the isolated bladder to obtain a preexperiment weight;

(c) exposing the isolated bladder to a solution containing a test compound under conditions for a time sufficient for the test compound to agonize or antagonize the Aquatic polyvalent cation-sensing receptor present in the isolated bladder; and

(d) weighing the bladder after the experimental period to obtain a post-experiment weight (the difference of pre and post experiment weights of the bladder are an indication of water reabsorption).

ACTIVITY - Anabolic; Homeostatic.

Winter and Summer Flounder can be grown and maintained in recycling water systems. Groups of both winter (Pleuronectes americanus) and summer (Paralichthus dentalus) flounder were maintained in multiple modular recycling water system units. Salinity survival limits for winter and summer flounder with a constant ratio of divalent and monovalent ions were determined. The survival limit of both winter and summer flounder in waters of salinities greater than normal seawater (10 mM Ca2+, 50 mM Mg2+ and 450 mM NaCl) is water containing twice (20 mM Ca2+, 50 mM Mg2+ and 900 mM NaCI) the normal concentrations of ions present in normal seawater. In contrast, the survival limit of both winter and summer flounder in waters of salinity less than normal seawater is 10% seawater (1 mM Ca2+, 5 mM Mg2+ and 45 mM NaCl). Flounder grown and/or maintained in low and hypersalinities possess different fat contents and taste as compared to flounder maintained in normal sea water. Use of a fully recycling water system permits growth of flounder at vastly different salinities. Groups of flounder (n=10) were adapted over a 15 day interval and maintained at either low salinity (LS) (e.g. at 10% normal seawater), normal seawater (NS) or hypersalinity (HS) (e.g. 2.times. seawater) for intervals of 3 months, under otherwise identical conditions. Survival among the 3 groups were comparable (all greater than 80%) and there were no differences in the electrolyte content of their respective sera. Analyses of fillet muscle from summer flounder for total fat, protein and moisture content are given in the specification. Muscle from low salinity flounder contained approximately 30% higher fat content as compared to flounder maintained in normal seawater and approximately 70% greater fat content when compared to flounder maintained in 2.times. seawater (e.g. the fat of a flounder maintained in normal salinity was 40% greater than flounder maintained in twice seawater). These differences appear selective because no significant differences were observed in either muscle protein or moisture content. Furthermore, fillets were sampled in a blinded protocol where tasters (n=6) were offered either raw or cooked fillets without knowledge of salinity conditions. Tasters could distinguish little difference between the taste of fillets of individual fish from each specific salinity group. However, when asked to compare fillets from flounder grown at differing salinities, a majority (5/6) clearly distinguished a taste difference between fillets from fish maintained at 10% salinity describing them as sweet and buttery tasting with a soft consistency as compared to fillets from fish maintained at either normal seawater or 2 multiply seawater that were described as wild and fishy tasting with a firmer consistency. These data provides evidence that

finishing growth of winter flounder at different water salinities can be used to alter the taste and fat content of the resulting fillets in summer and winter flounder. Groups of tagged hatchery raised summer flounder obtained from identical broodstock were exposed to either 10% seawater or 2 multiply seawater for an interval of 3 months under conditions identical to that described above. There were no significant differences in either length or width in fish maintained 10% seawater or 2.times. seawater. However, there was a significant difference in the weights of the respective fish where 10% seawater fish weighted 80 +/-14% (n=10) more than summer flounder maintained in 2 multiply seawater. Moreover, the summer flounder maintained in 10% seawater were nearly twice (2.1 +/- 0.4 multiply n=6) as thick as compared to fish maintained in 2 multiply seawater. These data show that flounder maintained at different water salinities exhibit significant differences in the thickness of their fillets. Thus, flounder could be finished using water of differing compositions to alter the thickness of their fillets.

MECHANISM OF ACTION - Modulation of polyvalent cation-sensing receptor activity.

USE - (I) May be used (III) to screen candidate compounds that may be used to assist fish in adapting to changing ion concentrations by altering water intake, water absorption or urine output and/or for modulating the percentage of total fat, protein and moisture of muscle of the fish (claimed).

Dwg.0/0

L6 ANSWER 2 OF 2 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-163246 [21] WPIDS
CROSS REFERENCE: 1997-489640 [45]; 2003-874926 [81]
DOC. NO. CPI: C2002-050370
TITLE: New nucleic acid molecule encoding polyvalent cation-sensing receptor protein, useful for regulating adaptation of fish e.g. flounder to marine and fresh water environments, and to alter tissue or meat/muscle composition.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): BROWN, E M; HARRIS, H W; HEBERT, S C
PATENT ASSIGNEE(S): (BGHM) BRIGHAM & WOMENS HOSPITAL
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6337391	B1	20020108 (200221)*			83

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6337391	B1	CIP of	US 1996-622738	19960327
		CIP of	WO 1997-US5031	19970327
			US 1998-162021	19980928

PRIORITY APPLN. INFO: US 1998-162021 19980928; US 1996-622738 19960327; WO 1997-US5031 19970327

AN 2002-163246 [21] WPIDS
CR 1997-489640 [45]; 2003-874926 [81]
AB US 6337391 B UPAB: 20031216

NOVELTY - An isolated nucleic acid sequence (I) comprising a fully defined sequence (S1) of 4134 base pairs as given in the specification encoding polyvalent cation-sensing receptor protein (PVCR), especially Shark Kidney calcium receptor related protein-I (SKCaR-RP-I) that allows fish to sense ion concentrations with a fully defined sequence of 1027 amino acids as given in the specification or its complement, is new.

DETAILED DESCRIPTION - An isolated nucleic acid sequence (I) comprising:

(a) a fully defined sequence (S1) of 4134 base pairs as given in the specification;

(b) coding region of S1 encoding polyvalent cation-sensing receptor protein (PVCR), especially Shark Kidney calcium receptor related protein-I (SKCaR-RP-I) that allows fish to sense ion concentrations with a fully defined sequence of 1027 amino acids as given in the specification; or

(c) complement of (I), is new.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid sequence having at least 80% or 90% identity with (S1), or the coding region of (S1), and that encodes a

polypeptide that allows fish to sense ion concentrations, or that assists fish in adapting to changing ion concentrations by altering water intake, water absorption or urine output, and allows fish to modulate the percentage of total fat, protein and moisture of muscle;

(2) an isolated nucleotide sequence, i.e. RNA sequence that encodes PVCR;

(3) a probe that hybridizes under high stringency conditions to (S1) or its complement, where the stringent conditions comprise 0.5 X standard saline citrate (SSC), 0.1% sodium dodecyl sulfate (SDS) and at 65 deg. C, where the probe hybridizes to a nucleic acid that encodes a polypeptide that allows fish to sense ion concentrations;

(4) a vector comprising (I) or its hybridizable sequence;

(5) a host cell transformed with the above vector; and

(6) an cDNA purified from a clone deposited under ***ATCC*** No. ***209602***.

USE - (I) or its fragment is useful as a probe to isolate additional aquatic PVCR homologs. (I) is useful for producing receptor proteins which can be used for structure determination, to assay a molecule's activity on a receptor, and to obtain antibodies binding to the receptor; being sequenced to determine a receptor's nucleotide sequence which can be used, as a basis for comparison with other receptors to determine conserved regions, determine unique nucleotide sequences for normal and altered receptors, and to determine nucleotide sequences to be used as target sites for antisense nucleic acids, ribozymes, hybridization detection probes, or polymerase chain reaction (PCR) amplification primers; as hybridization detection probes to detect the presence of a native receptor and/or a related receptor in a sample; and as PCR primers to generate particular nucleic acid sequence regions, for e.g. to generate regions to be probed by hybridization detection probes. The aquatic PVCR allows the successful adaptation of fish, such as flounder, to marine and fresh water environments, and controls maturation and developmental stages in marine species. Modulating the expression of PVCR activates or inhibits PVCR mediated ion transport and endocrine changes that permit fish to adapt to fresh or salt water. Activating PVCR in epithelial cells increases or decreases salinity tolerance in aquatic species. Regulating salinity tolerance is useful to develop new species of marine fish that are easily adaptable to fresh water aqua culture. The methods are useful for altering body composition i.e. tissue composition or meat/muscle composition by modulating salinity of surrounding environment. Body composition altered include fat content, protein content, weight, thickness, moisture and taste. Maintaining aquatic species in higher salinity than normal reduces parasites and/or bacteria while maintaining the species in lower salinity reduces contaminants, e.g. antibiotics, hydrocarbons and/or amines. The species can be maintained in both environments, consecutively to reduce parasites, bacteria and contaminants.

Dwg.0/32

=> d l7 ibib abs 1

L7 ANSWER 1 OF 1 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-163246 [21] WPIDS

CROSS REFERENCE: 1997-489640 [45]; 2003-874926 [81]

DOC. NO. CPI: C2002-050370

TITLE: New nucleic acid molecule encoding polyvalent cation-sensing receptor protein, useful for regulating adaptation of fish e.g. flounder to marine and fresh water environments, and to alter tissue or meat/muscle composition.

DERWENT CLASS: B04 C06 D16

INVENTOR(S): BROWN, E M; HARRIS, H W; HEBERT, S C

PATENT ASSIGNEE(S): (BGHM) BRIGHAM & WOMENS HOSPITAL

COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6337391	B1	20020108 (200221)*			83

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6337391	B1 CIP of	US 1996-622738	19960327
	CIP of	WO 1997-US5031	19970327
		US 1998-162021	19980928

PRIORITY APPLN. INFO: US 1998-162021 19980928; US
1996-622738 19960327; WO
1997-US5031 19970327
AN 2002-163246 [21] WPIDS
CR 1997-489640 [45]; 2003-874926 [81]
AB US 6337391 B UPAB: 20031216
NOVELTY - An isolated nucleic acid sequence (I) comprising a fully defined sequence (S1) of 4134 base pairs as given in the specification encoding polyvalent cation-sensing receptor protein (PVCR), especially ***Shark*** ***Kidney*** ***calcium*** ***receptor*** ***related*** ***protein*** -I (SKCaR-RP-I) that allows fish to sense ion concentrations with a fully defined sequence of 1027 amino acids as given in the specification or its complement, is new.

DETAILED DESCRIPTION - An isolated nucleic acid sequence (I) comprising:

(a) a fully defined sequence (S1) of 4134 base pairs as given in the specification;

(b) coding region of S1 encoding polyvalent cation-sensing receptor protein (PVCR), especially ***Shark*** ***Kidney*** ***calcium*** ***receptor*** ***related*** ***protein*** -I (SKCaR-RP-I) that allows fish to sense ion concentrations with a fully defined sequence of 1027 amino acids as given in the specification; or

(c) complement of (I), is new.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid sequence having at least 80% or 90% identity with (S1), or the coding region of (S1), and that encodes a polypeptide that allows fish to sense ion concentrations, or that assists fish in adapting to changing ion concentrations by altering water intake, water absorption or urine output, and allows fish to modulate the percentage of total fat, protein and moisture of muscle;

(2) an isolated nucleotide sequence, i.e. RNA sequence that encodes PVCR;

(3) a probe that hybridizes under high stringency conditions to (S1) or its complement, where the stringent conditions comprise 0.5 X standard saline citrate (SSC), 0.1% sodium dodecyl sulfate (SDS) and at 65 deg. C, where the probe hybridizes to a nucleic acid that encodes a polypeptide that allows fish to sense ion concentrations;

(4) a vector comprising (I) or its hybridizable sequence;

(5) a host cell transformed with the above vector; and

(6) an cDNA purified from a clone deposited under ***ATCC*** No. ***209602*** .

USE - (I) or its fragment is useful as a probe to isolate additional aquatic PVCR homologs. (I) is useful for producing receptor proteins which can be used for structure determination, to assay a molecule's activity on a receptor, and to obtain antibodies binding to the receptor; being sequenced to determine a receptor's nucleotide sequence which can be used, as a basis for comparison with other receptors to determine conserved regions, determine unique nucleotide sequences for normal and altered receptors, and to determine nucleotide sequences to be used as target sites for antisense nucleic acids, ribozymes, hybridization detection probes, or polymerase chain reaction (PCR) amplification primers; as hybridization detection probes to detect the presence of a native receptor and/or a related receptor in a sample; and as PCR primers to generate particular nucleic acid sequence regions, for e.g. to generate regions to be probed by hybridization detection probes. The aquatic PVCR allows the successful adaptation of fish, such as flounder, to marine and fresh water environments, and controls maturation and developmental stages in marine species. Modulating the expression of PVCR activates or inhibits PVCR mediated ion transport and endocrine changes that permit fish to adapt to fresh or salt water. Activating PVCR in epithelial cells increases or decreases salinity tolerance in aquatic species. Regulating salinity tolerance is useful to develop new species of marine fish that are easily adaptable to fresh water aqua culture. The methods are useful for altering body composition i.e. tissue composition or meat/muscle composition by modulating salinity of surrounding environment. Body composition altered include fat content, protein content, weight, thickness, moisture and taste. Maintaining aquatic species in higher salinity than normal reduces parasites and/or bacteria while maintaining the species in lower salinity reduces contaminants, e.g. antibiotics, hydrocarbons and/or amines. The species can be maintained in both environments, consecutively to reduce parasites, bacteria and contaminants.

Dwg.0/32

=> d l8 ibib abs 1

L8 ANSWER 1 OF 2 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-874926 [81] WPIDS
CROSS REFERENCE: 1997-489640 [45]; 2002-163246 [21]
DOC. NO. CPI: C2003-246939
TITLE: Fish ***polyvalent*** ***cation*** - ***sensing*** ***receptor*** proteins, useful for assisting fish in adapting to changing ion concentrations by altering water intake and absorption, urine output or for modulating the fat, protein and moisture content of muscle.
DERWENT CLASS: B04 D16
INVENTOR(S): BROWN, E M; HARRIS, H W; HEBERT, S C
PATENT ASSIGNEE(S): (BGHM) BRIGHAM & WOMENS HOSPITAL
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003166908	A1	20030904	(200381)*		1

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003166908	A1 CIP of	US 1996-622738	19960327
	CIP of	WO 1997-US5031	19970327
	Div ex	US 1998-162021	19980928
	Div ex	US 2000-715538	20001117
		US 2001-16496	20011210

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2003166908	A1 Div ex	US 6337391

PRIORITY APPLN. INFO: US 1998-162021 19980928; US 1996-622738 19960327; WO 1997-US5031 19970327; US 2000-715538 20001117; US 2001-16496 20011210
AN 2003-874926 [81] WPIDS
CR 1997-489640 [45]; 2002-163246 [21]
AB US2003166908 A UPAB: 20031216
NOVELTY - Aquatic ***polyvalent*** ***cation*** - ***sensing*** ***receptor*** (PVCR) polypeptide (I), is new.
DETAILED DESCRIPTION - An isolated polypeptide (I) molecule having at least about 80 - 90% identity with:
(a) 6 defined amino acid sequences (A1-A6) given in the specification; or
(b) an amino acid sequence encoded by the defined nucleic acid sequences (N1-N6) given in the specification (the isolated polypeptide molecule:
(i) allows fish to sense ion concentrations;
(ii) assists fish in adapting to changing ion concentrations by altering water intake, water absorption or urine output; and/or
(iii) allows a fish to modulate the percentage of total fat, protein and moisture of muscle).
INDEPENDENT CLAIMS are also included for:
(1) an antibody (II) that specifically binds to (I); and
(2) screening (III) for Aquatic ***polyvalent*** ***cation*** - ***sensing*** ***receptor*** agonists and antagonists comprising measuring water reabsorption in isolated urinary bladder by:
(a) isolating flounder urinary bladder containing an Aquatic ***polyvalent*** ***cation*** - ***sensing*** ***receptor*** ;
(b) weighing the isolated bladder to obtain a preexperiment weight;
(c) exposing the isolated bladder to a solution containing a test compound under conditions for a time sufficient for the test compound to agonize or antagonize the Aquatic ***polyvalent*** ***cation*** - ***sensing*** ***receptor*** present in the isolated bladder; and
(d) weighing the bladder after the experimental period to obtain a post-experiment weight (the difference of pre and post experiment weights of the bladder are an indication of water reabsorption).
ACTIVITY - Anabolic; Homeostatic.
Winter and Summer Flounder can be grown and maintained in recycling water systems. Groups of both winter (Pleuronectes americanus) and summer (Paralichthus dentalus) flounder were maintained in multiple modular

recycling water system units. Salinity survival limits for winter and summer flounder with a constant ratio of divalent and monovalent ions were determined. The survival limit of both winter and summer flounder in waters of salinities greater than normal seawater (10 mM Ca2+, 50 mM Mg2+ and 450 mM NaCl) is water containing twice (20 mM Ca2+, 50 mM Mg2+ and 900 mM NaCI) the normal concentrations of ions present in normal seawater. In contrast, the survival limit of both winter and summer flounder in waters of salinity less than normal seawater is 10% seawater (1 mM Ca2+, 5 mM Mg2+ and 45 mM NaCl). Flounder grown and/or maintained in low and hypersalinities possess different fat contents and taste as compared to flounder maintained in normal sea water. Use of a fully recycling water system permits growth of flounder at vastly different salinities. Groups of flounder (n=10) were adapted over a 15 day interval and maintained at either low salinity (LS) (e.g. at 10% normal seawater), normal seawater (NS) or hypersalinity (HS) (e.g. 2.times. seawater) for intervals of 3 months, under otherwise identical conditions. Survival among the 3 groups were comparable (all greater than 80%) and there were no differences in the electrolyte content of their respective sera. Analyses of fillet muscle from summer flounder for total fat, protein and moisture content are given in the specification. Muscle from low salinity flounder contained approximately 30% higher fat content as compared to flounder maintained in normal seawater and approximately 70% greater fat content when compared to flounder maintained in 2.times. seawater (e.g. the fat of a flounder maintained in normal salinity was 40% greater than flounder maintained in twice seawater). These differences appear selective because no significant differences were observed in either muscle protein or moisture content. Furthermore, fillets were sampled in a blinded protocol where tasters (n=6) were offered either raw or cooked fillets without knowledge of salinity conditions. Tasters could distinguish little difference between the taste of fillets of individual fish from each specific salinity group. However, when asked to compare fillets from flounder grown at differing salinities, a majority (5/6) clearly distinguished a taste difference between fillets from fish maintained at 10% salinity describing them as sweet and buttery tasting with a soft consistency as compared to fillets from fish maintained at either normal seawater or 2 multiply seawater that were described as wild and fishy tasting with a firmer consistency. These data provides evidence that finishing growth of winter flounder at different water salinities can be used to alter the taste and fat content of the resulting fillets in summer and winter flounder. Groups of tagged hatchery raised summer flounder obtained from identical broodstock were exposed to either 10% seawater or 2 multiply seawater for an interval of 3 months under conditions identical to that described above. There were no significant differences in either length or width in fish maintained 10% seawater or 2.times. seawater. However, there was a significant difference in the weights of the respective fish where 10% seawater fish weighted 80 +/-14% (n=10) more than summer flounder maintained in 2 multiply seawater. Moreover, the summer flounder maintained in 10% seawater were nearly twice (2.1 +/- 0.4 multiply n=6) as thick as compared to fish maintained in 2 multiply seawater. These data show that flounder maintained at different water salinities exhibit significant differences in the thickness of their fillets. Thus, flounder could be finished using water of differing compositions to alter the thickness of their fillets.

MECHANISM OF ACTION - Modulation of ***polyvalent*** ***cation*** - ***sensing*** ***receptor*** activity.

USE - (I) May be used (III) to screen candidate compounds that may be used to assist fish in adapting to changing ion concentrations by altering water intake, water absorption or urine output and/or for modulating the percentage of total fat, protein and moisture of muscle of the fish (claimed).

Dwg.0/0